The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte BINIE V. LIPPS and FREDERICK W. LIPPS

MAILED
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U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Appeal No. 2006-2644
Application No. 10/047,945

ON BRIEF

Before SCHEINER, GRIMES, and LEBOVITZ, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a method of reducing serum IgE in a patient, which the examiner has rejected as nonenabled. We have jurisdiction under 35 U.S.C. § 134. We affirm.

Background

"IgE is a minor component of total immunoglobulins and it is implicated in allergies, which in some cases manifests as asthma. . . . Normal adults have 0.2 to 1.0 mg% of IgE. Currently 20% of the US population has higher than the normal range of IgE and the percentage is increasing every year." Specification, page 1.

"[I]mmunoglobulins and other proteins are almost always assayed from serum. There is a reported data that IgG and IgA were assayed from saliva of BALB/c mice. . . . There is no published data reporting the use of saliva for assay of IgE." Id., page 3. The specification discloses that IgE levels can be determined by assaying saliva. See id., page 9, line 13 to page 10, line 1.

The specification also reports that "in humans oral administration of a synthetic Lethal Toxin Neutralizing Factor (LTNF) designated LT-10 lowers IgE level." Id., page 5, lines 9-10.[1] LTNF is a protein isolated from opossum serum that neutralizes venom from a variety of poisonous snakes. See generally Lipps, U.S. Patent 5,576,297 (cited in the specification, page 5). LT-10 is a peptide that corresponds to the N-terminal ten amino acids of LTNF. Specification, page 5, lines 16-19.

The specification describes two experiments that form the apparent basis for the assertion that LT-10 lowers IgE levels. The experiments are described, in their entirety, as follows:

> Experiment 1: The pool of several human salivas was split into two parts. To one part equal volume of PBS was added and to the second part equal volume containing 1 mg/ml of LT-10 was added. The mixtures were incubated at 37 °C for one hour. IgE levels were assayed in both mixtures by usual ELISA test using anti-IgE. It was revealed that IgE level was much reduced in the mixture of saliva and LT-10, in comparison to the mixture of saliva and PBS. This shows the binding of LT-10 to IgE in saliva, the bound IgE is not detected by anti-IgE by ELISA test.
>
> Experiment 2: I placed one ml of water in my mouth and kept it for 15 minutes, after which the mixture with saliva and water was collected. Likewise I placed one ml of LT-10 containing 1 mg/ml and the mixture of saliva and LT-10 was collected. IgE levels were assayed in both mixtures by usual ELISA test. It was revealed that IgE level was much reduced in

[1] Appellants' "oral" administration appears to be the route usually referred to as "sublingual." See the specification, page 6, line 4 ("LT-10 can be given orally under the tongue.").

the mixture of saliva and LT-10, in comparison to the mixture of saliva and water. This shows that the binding of LT-10 to IgE in saliva in mouth.

Page 8, lines 11-23.

The specification also describes an experiment in which co-inventor Binie Lipps self-administered LT-10 (2 mg per day) alone or in combination with Glucotrol® (a diabetes treatment) and monitored levels of various proteins. See page 13. IgE levels are shown in Table 4 (page 15).[2]

Discussion

1. Claim construction

Claims 9-18 are on appeal. Claims 1-8 are also pending but have been withdrawn from consideration by the examiner. The claims have not been argued separately and therefore stand or fall together. Claim 9 is representative and reads as follows:

9. A method for reducing free serum IgE in a human, comprising

administering to said human an effective amount of a peptide comprising at least the first four amino acids from the N-terminal of SEQ.ID. NO:2 to reduce serum level of free IgE in said human.

SEQ ID NO:2 is a peptide having the sequence Leu-Lys-Ala-Met-Asp-Pro-Thr-Pro-Pro-Leu-Trp-Ile-Lys-Thr-Glu. Specification, page 5, lines 20-21. It corresponds to the fifteen amino acids at the N-terminus of LTNF. Id., lines 13-21. Thus, claim 9 is directed to a method of reducing the level of IgE in the serum of a human patient by

[2] Figure 1 also purports to show IgE levels measured in certain experiments. We do not credit the data shown in the figure, however, because the specification provides no explanation of what the figure shows or how the data were derived. The figure does not show the same data as Table 4: Table 4 shows seven different measurements for each experiment while the figure shows only a single value for each experiment. In addition, the numbers shown in the y-axis of the figure do not correspond to any of the values shown in Table 4. Since the specification provides no meaningful explanation of what the figure represents, the figure does not contribute to the sufficiency of the specification's disclosure.

administering a peptide comprising at least the sequence Leu-Lys-Ala-Met to the patient.

2. Enablement

The examiner rejected claims 9-18 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The examiner reasoned that Appellants' "US Patent numbers 5,576,297 and 5,744,449 [disclose] that a peptide identical to SEQ ID NO:2, as well as peptides comprising at least 3 amino acids of this sequence, have the biological property of inhibiting the lethal effects of venom from poisonous snakes. . . . As such, the prior art clearly demonstrates that the peptide of SEQ ID NO:2 as well as fragments of SEQ ID NO:2 were known to be inhibitors of metalloproteinases found in snake venom." Examiner's Answer, pages 5-6.

The examiner noted the experiments described in the specification purportedly showing that LT-10 reduces IgE levels, but concluded that the data do not support that conclusion:

> SEQ ID NO:1 [LT-10] is a metalloproteinase inhibitor that is 10 amino acids in length. It is not an enzyme, so it would not be expected to have degraded the IgE present in the solution. . . . Since the epitope recognized by the anti-IgE antibody used by appellant is not specified, the only logical way that peptide binding to IgE could render the IgE undetectable is if the peptide masks the epitope on IgE recognized by the anti-IgE antibody. If this is so, peptide binding does not reduce IgE levels since IgE would still be detectable if an anti-IgE polyclonal sera or an anti-IgE antibody that recognizes a different epitope is used in the detection assay.

Id., pages 7-8. The examiner concluded that the data in Table 4 suffer from the same problem. He concluded that undue experimentation would be required to reduce IgE levels via the claimed method.

We agree with the examiner that the specification does not provide sufficient guidance to enable the claimed method. In particular, the specification provides inadequate evidence to show that any fragments of SEQ ID NO:2 in fact reduce serum levels of IgE.

As the examiner has pointed out, the experimental data in the specification do not show that LT-10 causes any reduction in the levels of IgE. The ELISA test used in the specification's experiments to measure IgE levels is based on antibody binding to the IgE. See the paragraph bridging pages 9-10. Thus, the assay does not measure whether an analyte is or is not present; all the assay can determine is whether the analyte is or is not bound by an antibody.

The results reported for the experiments in the specification (quoted at pages 2-3 above) are consistent with this limitation of ELISA tests. In Experiment 1, the data were reported to show that "the bound IgE is not detected by anti-IgE by ELISA test" and the results of Experiment 2 were said to show "the binding of LT-10 to IgE in saliva in mouth." Specification, page 8. We agree with the examiner that, at best, the data show that LT-10 binds the same part of the IgE molecule that is bound by the antibody used in the ELISA test. The data do not show that the binding of LT-10 to IgE results in a reduction in the amount of IgE present.

In addition, Appellants have pointed to no evidence showing the effect of LT-10 on serum IgE levels. Claim 9 is directed to a "method for reducing free serum IgE in a human" by administering a peptide "to reduce serum level of free IgE in said human" (emphases added). The specification provides no evidence to show that the level of IgE

in saliva, which is what is measured in the working examples, correlates to the level of free IgE in serum.

The specification shows that IgE can be measured in saliva but provides no evidence to show that the level measured in saliva is indicative of the level of free IgE in serum. Nor have Appellants pointed to any other evidence of record or known to those skilled in the art that supplies the missing correlation. In fact, the specification states that "[f]or humans, immunoglobulins and other proteins are almost always assayed from serum. . . . There is no published data reporting the use of saliva for assay of IgE and other proteins." Page 3. Thus, the evidence of record is not adequate to support the assertion that saliva levels of IgE provide an accurate measure of free serum levels of IgE.

Finally, Appellants have pointed to no evidence showing that any fragments of SEQ ID NO:2 smaller than 10 amino acids have any effect on IgE levels. The working examples in the specification were carried out with LT-10, a peptide ten amino acids long. No data are presented for any other peptide. Appellants have acknowledged that "[f]ree-IgE reduction with a peptide is not known." Appeal Brief, page 7. Thus, those skilled in the art would not assume, based on the state of the art, that fragments of LT-10 would also bind to IgE.

For these reasons, we agree with the examiner that the specification does not provide adequate guidance to enable those skilled in the art to practice the claimed method – reducing the serum level of IgE in a human by administering a peptide comprising the first four amino acids of SEQ ID NO:2 – without undue experimentation. We therefore affirm the rejection for lack of enablement.

Appellants argue that the examiner has not considered all of the Wands factors. See the Appeal Brief, pages 5-6. Appellants argue that the examiner has improperly focused on "the credibility of the working examples" (id., page 5) and that "[w]hether or not the data is believable or credible is a utility issue, not an enablement issue" (id., page 8).

We do not find this argument persuasive. A rejection for lack of enablement can "take[ ] several forms." In re Cortright, 165 F.3d 1353, 1356, 49 USPQ2d 1464, 1466 (Fed. Cir. 1999). Most commonly, "[t]he PTO will make a scope of enablement rejection where the written description enables something within the scope of the claims, but the claims are not limited to that scope." Id. "On the other hand, if the written description does not enable any subject matter within the scope of the claims, the PTO will make a general enablement rejection, stating that the specification does not teach how to make or use the invention." Id.

The examiner's rejection in this case is of the latter type. "The PTO cannot make this type of rejection, however, unless it has reason to doubt the objective truth of the statements contained in the written description." Id. at 1357, 49 USPQ2d at 1466. As discussed above, the specification itself provides evidence that casts doubt on the statement that fragments of SEQ ID NO:2 reduce serum levels of IgE: there is no evidence that LT-10 reduces IgE levels, as opposed to masking IgE from antibody binding; there is no evidence that the level of IgE measured in saliva corresponds to that in serum; and there is no evidence that fragments of SEQ ID NO:2 smaller than ten amino acids have any IgE-binding activity.

Appellants also argue that additional data to support the examples cannot properly be required because "what is presented is human clinical data. The only way to statistically verify its validity is by providing more human clinical data. And that, in essence, is a requirement for human clinical trials which is clearly outside the law." Appeal Brief, pages 8-9.

This argument is also unpersuasive. The evidence needed to show that the claimed method is enabled can take a variety of forms. For example, in vitro studies showing that LT-10 causes degradation of IgE would provide evidence that LT-10 can reduce IgE levels in vivo. Animal studies, in an art-recognized animal model, showing that IgE levels measured in saliva correlate to serum IgE levels would provide evidence to help show that the specification's working examples support the claimed method. Evidence that a four amino acid long fragment of SEQ ID NO:2 has the same effect (in vitro or in an animal model) as LT-10 would help support the breadth of the current claims. In short, human clinical trials are not required to show enablement, and the examiner is not implicitly requiring them.

In summary, the specification provides inadequate evidence to show that any fragment of SEQ ID NO:2 would have the effect of reducing the level of free serum IgE if administered to a human. Since the specification does not adequately enable any embodiment within the scope of the claims, it logically follows that it fails to enable practice of the full scope of the claims without undue experimentation. The examiner did not err in omitting a detailed discussion of the Wands factors. We affirm the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

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